IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of
Keiji KUBO, et al. Group Art Unit: 1625
Serial No.: 11/596,089 Examiner: CHANG, CELIA C.
Filed: November 9, 2006
For: CYCLIC AMIDE DERIVATIVE, AND ITS PRODUCTION AND USE

VERIFICATION OF ENGLISH TRANSLATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Tadayuki MOTOYAMA, declare that I am conversant in both the Japanese and English languages and that the English translation as attached hereto is an accurate partial translation of JP 5-208946 A1 published on August 20, 1993.

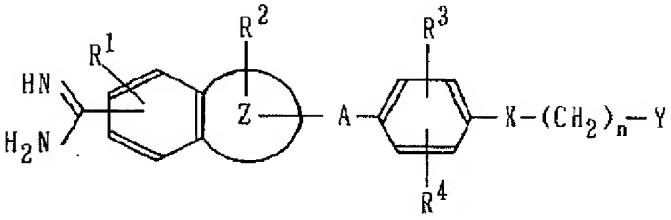
Signed this 27th day of August, 2009.

Tadayuki Motoyama

Tadayuki MOTOYAMA

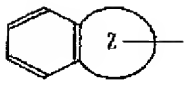
[Claims]

1. An aromatic amidine derivative represented by the formula (I):



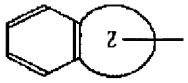
(I)

wherein R^1 represents a hydrogen atom or a lower alkoxy group, R^2 represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, carboxyl group, alkoxycarbonyl group, carboxyalkyl group or alkoxycarbonylalkyl group, R^3 represents a hydrogen atom, carboxyl group, alkoxycarbonyl group, carboxyalkyl group, alkoxycarbonylalkyl group, carboxyalkoxy group or alkoxycarbonylalkoxy group, R^4 represents a hydrogen atom, hydroxy group, a lower alkyl group or a lower alkoxy group, n represents an integer of 0 to 4, A represents a C_{1-4} alkylene group optionally substituted with 1 to 2 of hydroxyalkyl, carboxyl, alkoxycarbonyl, carboxyalkyl or alkoxycarbonylalkyl, X represents a single bond, oxygen atom, sulfur atom or carbonyl group, Y represents an optionally substituted saturated or unsaturated 5- to 6-membered heterocyclic group or cyclic hydrocarbon group, an optionally substituted amino group or an optionally substituted aminoalkyl group, the group represented by



represents a group selected from indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, naphthyl, tetrahydronaphthyl and indanyl, or a salt thereof.

2. The aromatic amidine derivative or a salt thereof according to claim 1, wherein the group represented by



is a group selected from benzofuranyl, benzimidazolyl, indolyl, benzothienyl, benzothiazolyl, naphthyl and tetrahydronaphthyl.

3. The aromatic amidine derivative or a salt thereof according to claim 1, wherein the saturated or unsaturated 5- to 6-membered heterocyclic group is those containing 1 to 2 of nitrogen atom or oxygen atom as heteroatoms.

4. 2-[4-[(1-acetimidoyl-3-pyrrolidinyl)oxy]phenyl]-3-(7-amidino-2-naphthyl)propionic acid or a salt thereof.

5. (+)-2-[4-[((3S)-1-acetimidoyl-3-pyrrolidinyl)oxy]phenyl]-3-(7-amidino-2-naphthyl)propionic acid or a salt thereof.

6. (2S)-2-[4-[((3S)-1-acetimidoyl-3-pyrrolidinyl)oxy]phenyl]-3-(7-amidino-2-naphthyl)propionic acid or a salt thereof.

7. (2R)-2-[4-[((3R)-1-acetimidoyl-3-

pyrrolidinyl)oxy]phenyl]-3-(7-amidino-2-naphthyl)propionic acid or a salt thereof.

8. 2-[4-[(1-acetimidoyl-2-pyrrolidinyl)methoxy]phenyl]-3-(5-amidinobenzo[b]thien-2-yl)propionic acid or a salt thereof.

9. (+)-2-[4-[((2S)-1-acetimidoyl-2-pyrrolidinyl)methoxy]phenyl]-3-(5-amidinobenzo[b]thien-2-yl)propionic acid or a salt thereof.

10. 2-[4-[(1-acetimidoyl-4-piperidinyl)oxy]phenyl]-3-(7-amidino-2-naphthyl)propionic acid or a salt thereof.

11. (+)-2-[4-[(1-acetimidoyl-4-piperidinyl)oxy]phenyl]-3-(7-amidino-2-naphthyl)propionic acid or a salt thereof.

12. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 1 as an active ingredient.

13. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 2 as an active ingredient.

14. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 3 as an active ingredient.

15. A blood coagulation inhibitor or a prophylactic or

therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 4 as an active ingredient.

16. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 5 as an active ingredient.

17. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 6 as an active ingredient.

18. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 9 as an active ingredient.

19. A blood coagulation inhibitor or a prophylactic or therapeutic agent for thrombus or embolus, which comprises the compound or a salt thereof according to claim 11 as an active ingredient.

Column 17, paragraph [0035]

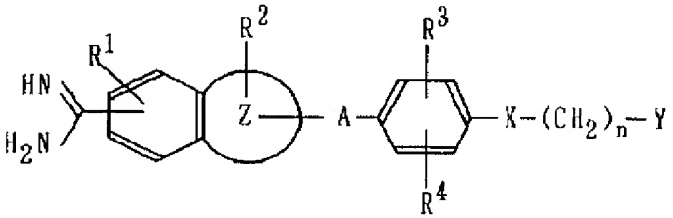
[Effects of the Invention]

The compound of the present invention exerts an anticoagulant activity based on excellent FXa inhibitory

action. Therefore, without any action on platelet, the compound of the present invention can treat or prevent various diseases caused by thrombus and embolus such as cerebral infarction, cerebral thrombosis, cerebral embolism, transient ischemic attack (TIA), myocardial infarction, unstable angina, pulmonary infarction, pulmonary embolism, Buerger's disease, deep vein thrombosis, disseminated intravascular coagulation, thrombus formation after blood vessel prosthesis implantation and artificial valve replacement, reocclusion after revascularization such as percutaneous transluminal coronary angioplasty (PTCA), percutaneous transluminal coronary recanalization (PTCR), and the like, thrombus formation during extracorporeal circulation, and the like.

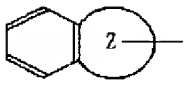
[Abstract]

[Constituent] An anticoagulant agent whose active ingredient is an aromatic amidine derivative represented by the following formula (I) or a salt thereof.



(1)

wherein the group represented by



represents a group selected from indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, naphthyl, tetrahydronaphthyl and indanyl, X represents a single bond, oxygen atom, sulfur atom or carbonyl group, Y represents an optionally substituted saturated or unsaturated 5- to 6-membered heterocyclic group or cyclic hydrocarbon group, an optionally substituted amino group or an optionally substituted aminoalkyl group.

[Effect] This compound exerts an anticoagulant activity based on an excellent FXa inhibitory action.